

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 September 2005 (22.09.2005)

PCT

(10) International Publication Number
WO 2005/087745 A1

(51) International Patent Classification⁷: **C07D 221/12**,
A61K 31/473, C07D 401/12, 471/04

SZ, TD, TG only: HATZELMANN, Armin; Alter Wall 3, 78467 Konstanz (DE). ZITT, Christof; Mainaustr. 209 D, 78464 Konstanz (DE).

(21) International Application Number:
PCT/EP2005/051054

(72) Inventor (for AE, AG, AL, AM, AT, AU, AZ, BA, BB, BE, BF, BG, BJ, BR, BW, BY, BZ, CF, CG, CH, CI, CM, CN, CO, CR, CU, CY, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FR, GA, GB, GD, GE, GH, GM, GN, GQ, GR, GW, HR, HU, ID, IE, IL, IN, IS, IT, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MC, MD, MG, MK, ML, MN, MR, MW, MX, MZ, NA, NE, NI, NL, NO, NZ, OM, PG, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL only): **BARSIG, Johannes**; Bleichenweg 11, 78467 Konstanz (DE).

(22) International Filing Date: 9 March 2005 (09.03.2005)

(72) Inventors (for BE, BF, BJ, CF, CG, CI, CM, CY, FR, GA, GN, GQ, GR, GW, IE, IT, MC, ML, MR, NE, NL, SI, SN, SZ, TD, TG, VN, YU, ZA, ZM, ZW only): MARX, Degenhard; Obere Reute 15, 78345 Moos (DE). KLEY, Hans-Peter; Im Weinberg 3b, 78476 Allensbach (DE).

(25) Filing Language: English

(72) Inventor; and

(26) Publication Language: English

(75) Inventor/Applicant (for US only): KAUTZ, Ulrich [DE/DE]; Prof.-Schmider-Str. 12, 78476 Allensbach (DE).

(30) Priority Data:
04100990.3 10 March 2004 (10.03.2004) EP
04106677.0 17 December 2004 (17.12.2004) EP

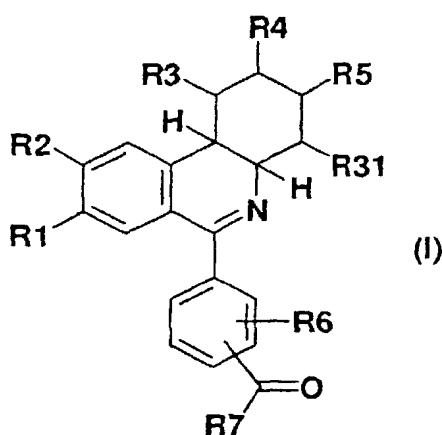
(74) Agents: WILD, Robert et al.; c/o Altana Pharma AG, Byk-Gulden-Str. 2, 78467 Konstanz (DE).

(71) Applicant (for all designated States except US): ALTANA PHARMA AG [DE/DE]; Byk-Gulden-Str. 2, 78467 Konstanz (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

[Continued on next page]

(54) Title: NOVEL AMIDO-SUBSTITUTED HYDROXY-6-PHENYLPHENANTHRIDINES AND THEIR USE AS PDE4 INHIBITORS



(57) Abstract: Compounds of formula (I) in which R1 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-4C-alkoxy, R2 is hydroxyl, 1-4C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, 2,2-difluoroethoxy, or completely or predominantly fluorine-substituted 1-4C-alkoxy, or in which R1 and R2 together are a 1-2C-alkylenedioxy group, R3 is hydrogen or 1-4C-alkyl, R31 is hydrogen or 1-4C-alkyl, either, in a first embodiment (embodiment a) according to the present invention, R4 is -O-R41, in which R41 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy-1-4C-alkyl, hydroxy-2-4C-alkyl, 1-7C-alkylcarbonyl, or completely or predominantly fluorine-substituted 1-4C-alkyl, and R5 is hydrogen or 1-4C-alkyl, or, in a second embodiment (embodiment b) according to the present invention, R4 is hydrogen or 1-4C-alkyl, and R5 is -O-R51, in which R51 is hydrogen, 1-4C-alkyl, 1-4C-alkoxy-1-4C-alkyl, hydroxy-2-4C-alkyl, 1-7C-alkylcarbonyl, or completely or predominantly fluorine-substituted 1-4C-alkyl, R6 is hydrogen, halogen, 1-4C-alkyl or 1-4C-alkoxy, either, in a first aspect (aspect 1) according to the present invention, R7 is -N(R8)R9, or, in a second aspect (aspect 2) according to the present invention, R7 is

-NH-N(R18)R19, are novel effective PDE4 inhibitors.

WO 2005/087745 A1



PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) **Designated States (unless otherwise indicated, for every kind of regional protection available):** ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,

PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— of inventorship (Rule 4.17(iv)) for US only

Published:

- with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.